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A peer-driven intervention to help patients resume CPAP therapy following discontinuation: a multicenter, randomized clinical trial with patient involvement

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A peer-driven intervention to help patients resume CPAP therapy following discontinuation: a multicenter, randomized clinical trial with patient involvement

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ABSTRACT

Introduction

Obstructive Sleep Apnoea Syndrome (OSAS) is one of the most common chronic diseases. It may be associated with symptoms of excessive daytime sleepiness and neurocognitive and cardiovascular complications. First line therapy for OSAS involves home Continuous Positive Airway Pressure (CPAP), however nearly half of patients do not adhere with this treatment over the long-term. Cognitive-behavioural interventions that include health professionals and patient and public involvement (PPI) are increasingly advocated in the fields of education and research. We hypothesize that a peer-driven intervention could help patients with OSAS to resume CPAP use after discontinuation.

Methods and analysis

We have designed a prospective, multicentre randomized, controlled trial that will be co-conducted by health professionals, a home provider of CPAP and patients as experts or peers or participants. The primary aim is to evaluate the impact of a 6-month, peer-driven intervention to promote the resumption of CPAP after discontinuation. We anticipate that 20% of patients in the intervention group will reuse CPAP as compared to 6% in control group, thus 104 patients must be included in each group. The secondary aims are i) to evaluate the impact of the peer-driven intervention on adherence to CPAP compared to the control group (mean adherence and percentage of nights with at least 4 hours' use /night for 70% of nights); - ii) to determine factors associated with resumption of CPAP; -iii) to assess patient satisfaction with the peer-driven intervention at 6 months; -iv) to evaluate the feasibility and the execution of the peer-driven intervention and peer satisfaction. Adult outpatients with an established diagnosis of severe OSA (Apnea-Hypopnea Index >30 events/hour) that have stopped using CPAP within 4 to 12 months after initiation will be recruited. The peers who will perform the intervention will be patients with OSAS treated with CPAP with good adherence (at least 4 hours/night, 70% of nights) and trained in

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motivational enhancement and cognitive-behavioural therapies. Trained peers will conduct 3 interviews within 6 months with participants.

Ethics and dissemination

Ethical approval has been obtained from the French Regional Ethics Committee CPP Ouest II-Angers, (IRB 21.02.25.68606 (2021/25)). All participants will sign written informed consent. The results will be presented at conferences and published in peer-reviewed journals as well as public media.

Trial registration number: NCT04538274

Strengths and limitations of this study

- Patient involvement (PI) from the beginning of the setup of this trial. RM, the first author, is a patient expert who has completed a PhD devoted to the roles of patients in the health care system.
- The need to help patients to resume CPAP after discontinuation is currently unmet. There is a robust rationale supporting the use of motivational enhancement and cognitive-behavioural therapies performed by peers to promote CPAP resumption.
- Patient-peers with OSAS who are compliant with CPAP are probably the best stakeholders to help non-compliant patients to resume CPAP.
- Our team has experience in patient and public involvement (PPI) from work undertaken in the Grenoble Alpes University Hospital and the Grenoble Alpes University Department of Patients.

Key words: patient and public involvement (PPI), obstructive sleep apnoea syndrome (OSAS), excessive daytime sleepiness, non-adherence, motivational enhancement and cognitive-behavioural therapies

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Abbreviations and website addresses

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| AGIR à dom. | Home care and services, Meylan, France, https://www.agiradom.com/en/ |
| AHI | Apnoea + Hypopnea Index |
| CPAP | Continuous Positive Airway Pressure |
| DUPGA | Département Universitaire des Patients Grenoble Alpes: Grenoble Alpes University Department of Patients, DUPGA@univ-grenoble-alpes.fr |
| EDS | Excessive Daytime Sleepiness |
| OSAS | Obstructive Sleep Apnoea Syndrome |
| PI | Patient Involvement |
| PPI | Patient and Public Involvement |

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INTRODUCTION

Obstructive Sleep Apnoea syndrome (OSAS) is one of the most common chronic diseases. It is characterized by recurrent episodes of upper airway collapse during sleep, and may or may not be associated symptoms of excessive daytime sleepiness (EDS) and neurocognitive and cardiovascular complications [1]. Twelve million adults aged between 30 and 69 years may have moderate to severe OSAS in France, based on an Apnoea Hypopnea Index (AHI) threshold value of 15 or more events per hour of sleep [2]. The risks associated with the disease can be severe, for example, individuals with untreated OSAS have a three times greater risk of motor vehicle accidents than the general population [3]. OSAS is also associated with an increased risk of cardiovascular disease, diabetes and glucose dysregulation [4], independent from obesity [5].

The first line therapy for OSAS is continuous positive airway pressure (CPAP) [1,6,7]. CPAP has been shown to effectively reduce EDS and to improve daily functioning, cognitive function, mood and quality of life [3,6]. The use of CPAP also reduces traffic accidents [7] and other work-related injuries, and improves work productivity [8]. Although CPAP therapies are highly effective in normalizing AHI and reducing symptoms in symptomatic patients, treatment success is limited by long term nonadherence in nearly half of patients [9]. Technical progress in the systems and interfaces (soundproofing, improved masks, humidification, pressure modulation, etc.) have unfortunately not been sufficient to improve compliance [10,11]. Equally, the effect sizes of telemedicine approaches are not as large as what has been achieved with the use of behavioural therapies, and the impacts on patient and provider satisfaction and cost-effectiveness are not yet clear [12–15].

Nonadherence is related to users' profiles, their representations of OSAS and the benefits they experience from CPAP [12,16,17]. This is why cognitive-behavioural and motivation enhancement therapies conducted by health professionals could be effective in

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ensuring adherence to CPAP. A Cochrane review in 2014 showed that there is a low level of evidence that such interventions increase CPAP use (by 1.44 h per night in six studies; n = 584) and increase the number of participants who used their devices for longer than four hours per night (from 28 to 47% in 3 studies; n= 358)[18]. More robust studies are thus needed to increase the level of evidence regarding these types of interventions.

In addition, patient and public involvement (PPI) is more and more advocated in the fields of health education and research [19–25]. Nevertheless, the efficacy of PPI remains to be demonstrated [26]. To our knowledge, only one previous pilot study in 39 patients showed that one-to-one peer support at CPAP initiation was feasible and generated high patient satisfaction. However, the study was not powerful enough to demonstrate effectiveness in terms of adherence to CPAP [18,27]. The data from the study, are, however, useful for designing further studies.

The aim of this adequately powered randomized clinical trial is therefore to assess the role of trained Patient Involvement (PI) representatives to help patients with OSAS to restart CPAP after discontinuation.

METHODS AND ANALYSIS

Study design

This is a prospective, multicentre, randomized controlled trial that will be co-conducted by health professionals, a CPAP home provider and patients as experts or peers or participants. After signing a consent form, patients' participants will be randomized 1:1 to the intervention group with peers or the control group. *Nota bene:* the peers involved in the conduct of the study will sign a confidentiality agreement of non-divulgence of the information exchanged with the participants.

Objectives

Primary research aim

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The primary aim is to evaluate the impact of a 6-month intervention involving trained PI representatives to promote the resumption of CPAP in patients who have discontinued its use. Resumption of CPAP is defined as the medical prescription and the setting up of a new CPAP device at home by the homecare provider.

Secondary research aims:

- i) to evaluate the impact of the peer-driven intervention on adherence to CPAP by comparing adherence with the control group (mean adherence and % of nights with at least 4 hours' use /night for 70 % of nights);
- ii) to determine the factors associated with the resumption of CPAP treatment;
- iii) to assess the satisfaction of the intervention group with the peer-driven intervention at 6 months;
- iv) to evaluate the feasibility and the execution of the peer-driven intervention and the satisfaction of peers after the interviews conducted.

Patients, Table 1

Adults with an established diagnosis of severe OSAS (AHI >30 events/hour) who have discontinued CPAP by returning their device to the homecare provider within 4 to 12 months after CPAP initiation will be recruited according to the study flow chart depicted in Figure 1.

Interventions (Figure 1)

Recruitment and training of PI representatives

PI representatives will be recruited from the investigators clinics. To be recruited as a PI representative, patients should:

- have used home CPAP for at least one year,
- have a CPAP adherence of at least 4 h/night for 70% of nights,

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- express their motivation in participating in a training and orientation session conducted by research staff and including expert patients from the Grenoble Alpes University Department of Patients (DUP GA) [28],

- accept to conduct 3 motivational sessions by videoconference meetings of 45 to 60 minutes duration with 5 to 8 patients within 6 months after each patient's inclusion,

Patients with any major psychiatric illness, shift-workers or frequent out of town travellers will not be recruited as peers.

Peers will be trained during a three half-days interactive session organised by DUP GA, with experts in patient therapeutic education and communication, and investigators [28].

Peers will be taught how to interact with the patients recruited in the study: the aim is for them to share their experiences but not to provide any medical advice.

Description of the intervention

Trained peers will meet patients randomized into the intervention group by videoconference. Each PI representative will be allocated 5 to 8 patients. They will conduct 3 face to face motivational sessions, each of 45 to 60 minutes duration, over a 6-month period based on the principle of motivational enhancement and cognitive-behavioural therapies [11,13]. The content of the first session is designed to identify and understand the underlying reasons for stopping CPAP treatment and to identify difficulties encountered by the patient (advantages and disadvantages of CPAP treatment). The aim of the second session will be for the patient to define his/her objectives and priorities. During the last session, will be discussed to strengthen the motivation to change and how to plan for it. The peers will receive 100 € per patient for the 3 interviews.

In the control group, patients will be informed, at inclusion, that they can have a visit with a physician investigator at any time to resume treatment if they wish, as is usual practice.

At the end of the six-month follow-up period, all patients in both groups will have a consultation with their physician who will suggest they resume CPAP treatment. This visit

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may take place earlier if the patient wishes to resume CPAP treatment before the end of the follow-up period.

Assessment

Average adherence to CPAP will be measured from data recorded by the built-in software of the CPAP devices (via tele monitoring or retrieved by a home technician) for 1 month after the final consultation.

The relationship between the variables below and a positive response to the peers intervention (defined by a restart of CPAP treatment) will be analyzed: age, sex, Body Mass Index (BMI), marital status, education level, socio-professional status, precariousness (using the EPICES score), smoking and alcohol use, comorbidities (using Charlson score), history of OSAS (date of diagnosis of OSAS, baseline AHI), observance to treatments (Girerd score), date and reason for stopping CPAP and EDS score (using the Epworth Sleepiness Scale).

To determine patient profiles, their representations of OSAS, their experiences with CPAP and their knowledge and confidence to manage their health, 3 questionnaires will be completed at inclusion (M0) and at the 6-month follow-up (M6): the Functional Outcomes of Sleep Questionnaire (FOSQ) a disease-specific quality of life questionnaire [29], the Patient Activation Measure (PAM) a measure that assesses patient knowledge, skill, and confidence for self-management [30] and the Self-Efficacy Measure for Sleep Apnea (SEMSA) [31,32] a tool with strong psychometric properties that identifies patient perceptions that may indicate those most likely not to adhere to treatment.

The satisfaction of participating patients with the PI intervention and the satisfaction of PI representatives will be measured on a 4-point Likert scale: very dissatisfied, dissatisfied, satisfied, very satisfied.

Finally, the feasibility and the execution of the 3 interviews will be assessed by the number of interviews carried out in their entirety and the average duration of each

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2 interview (in minutes).

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4 All information will be collected in secure electronic medical records in accordance with
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6 the requirements of General Data Protection Regulation.

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9 **Statistical analysis**

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11 *Sample size*

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13 We hypothesize that 20% of patients allocated to the intervention group will reuse CPAP
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15 6 months as compared to 6% of patients in the control group. A two group χ^2 test with a
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17 5% two-sided significance level will have 80% power to detect such difference between
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19 the two groups when the sample size in each group is 90 (nQuery v8, Statistical
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21 Solutions, Cork, Ireland). In order to take into account a possible drop-outs and to comply
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23 with the intent-to-treat principle, we will inflate the sample size by a factor of 15% [33].
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25 We thus plan to include 104 patients per group (i.e. 208 patients in total). 15 patient peers
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27 will be involved.

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32 *Feasibility and recruitment*

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34 The home care provider, *AGIR à dom.* follows more than 20,000 patients with OSAS
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36 who use CPAP in the south of France. In 2018, out of 3,281 patients who started CPAP
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38 within the study area (Isère, Savoie and Haute-Savoie), 365 discontinued it between 4 to
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40 12 months post initiation and 6% resumed use within 6 months after discontinuation.

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43 *Randomization*

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45 After consent, randomization will be performed by a centralized computer software for
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47 each investigating center. It will be stratified on the center.

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50 **Statistical analysis plan**

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53 *Descriptive analyses:* continuous variables will be expressed as medians (25th/75th
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55 percentiles) or means (SD) depending on normality which will be assessed with the
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57 Shapiro-Wilk test. Categorical variables will be reported as absolute numbers and
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59 percentages for both groups. Baseline comparisons between groups will be made using a
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Student's t-test or Mann-Whitney U test, depending on the distribution. For discrete variables, a χ^2 test will be used. If significant differences are observed between arms, ANOVA and multivariable regression will be performed. In the case of missing data, an imputation strategy will be applied according to the percentage of missing values. Data management and statistical analyses will be performed using SAS, V.9.4, SAS Institute.

Primary outcome analysis: the impact of the PI intervention on the resumption of CPAP treatment will be studied by comparing the resumption of CPAP in the 2 arms, using a Chi-square test. To take into account a possible centre effect, a second analysis will be carried out using a conditional logistic regression stratified by the centre; the intervention or control arm will be considered as the dependent variable.

Secondary outcomes analyses: mean CPAP compliance one month after resumption of CPAP will be analysed using a mixed linear model (fixed factor: randomisation arm (intervention vs. control), random factor: centre). Comparison of the probability of resuming CPAP with an average compliance of at least 4 hours/night, 70% of nights between the intervention and control groups will be analysed using a conditional logistic regression, stratified by centre. All analyses will be performed as intention-to-treat and then a sensitivity analysis will also be performed *per protocol* (patients who have not resumed treatment will be considered to have zero adherence).

The association between resumption of CPAP and the sociodemographic parameters, clinical data and the scores of the three questionnaires will be studied by conditional logistic regression models stratified by centre, and adjusted by arm (intervention vs control).

In the intervention arm, descriptive statistics will be presented on the satisfaction as well as on the number of interviews carried out and their average duration.

Ethics

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2 The study will be conducted in accordance with the Declaration of Helsinki and the
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4 recommendations for Good Clinical Practice. Written informed consent will be signed by
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6 all study participants before enrolment in the study. Patients will have the right to withdraw
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8 from the study without incurring any prejudice at any time.
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11 **Patient involvement**

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13 RM, first author and expert patient, and members of DUP GA participated in the design of
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15 this study and will participate in all stages including teaching peers [28] and promoting
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17 and reporting the data, including publication in peer review. Thanks to training with health
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19 professionals and expert patients [22,23,25] peers will adopt the appropriate posture to
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21 enable patients to find their own resources to overcome barriers to use CPAP.
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25 **Dissemination**

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27 Dissemination plans of the results include presentations at conferences and a publication
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29 in peer-reviewed journal. Updates of the randomized trial will be available at
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31 ClinicalTrials.com. All patients will be informed that the dissemination of results will be
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33 accessible on request.
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37 **Sponsor and funding**

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39 The study sponsor will be AGIR à dom. Co-Principal investigators are RM, an expert
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41 patient, and JCB, a researcher. The collaborators and sponsors were not involved in the
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43 design of the study and will not influence the execution, analysis or publication of results.
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49 **DISCUSSION**

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51 OSAS is associated with many negative health consequences [1]. The lack of compliance
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53 with home CPAP therapy, which is the first line of treatment, and which has shown to be
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55 effective on quality of life is a major issue both in terms of the patient's own health status
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57 and in health care utilisation [1,2,7,8]. Attempts have been made to improve CPAP
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59 compliance by improving technical issues relating to the comfort of use of the system
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[10,11] and the use of the of remote monitoring and telemedicine, along with the implementation of web-based adherence interventions [12–15]; however they have not been shown to improve compliance with the therapy. Other strategies to improve compliance therefore need to be developed and tested.

One of the main strengths of this study is the involvement of peers in the implementation of the behavioural intervention. Regarding efficacy, the involvement of patients with experience in the motivation of their peers to comply with treatment has been implemented with success in other chronic conditions requiring self-management such as HIV and diabetes [34,35]. Furthermore, evidence suggests that patients perceive peers with similar comorbidities as more credible than health-care professionals in the delivery of behavioural interventions [36–38]. The concept of PPI in education and research has been adopted by a growing number of medical schools, particularly in the United kingdom [19,24]. If the results of this study confirm the effectiveness of the PI intervention in promoting resumption of CPAP in patients initially failing CPAP, this study will provide an evidence base to support the use of PI in the management of OSAS in conjunction with the home healthcare provider and specialized sleep centers [39].

The aim to seek factors that are related to CPAP resumption will provide useful information regarding those patients who are more likely to resume CPAP and therefore who PI interventions are more likely to help. This will open the way for further studies to determine the most appropriate methods to improve compliance in those patients who benefit less from PI interventions.

Despite these strengths, the study has two main inherent limitations. Firstly, the results are likely to be biased by the fact that patients who accept to participate may be more likely to resume CPAP therapy than those who decline participation. The results may therefore not be generalizable to all patients who have stopped using their CPAP as prescribed. Secondly, the effectiveness of the intervention may also depend on the capacity of the peer-

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participant to deliver it. The training is quite short (3 half-days) and some of the peers recruited may be more skilled than others in providing such intervention. However, in this study, the peers will be additionally supported throughout the study by the University Department of Patients.

In summary, the results of this study will determine the effectiveness of a PI intervention to motivate patients who have stopped using their CPAP as prescribed to resume its use on compliance with CPAP therapy. The results will also provide information regarding the factors relating to resumption of CPAP, providing a starting point for further studies to determine the most appropriate methods to improve compliance in those patients who benefit less from PI interventions.

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Contributors RM participated in the design of the study, wrote the article based on the study protocol, will train PI, collect and analyse data into the protocol. CP participated in the design of the study, wrote the study protocol and will include patients into the protocol together with PPI. SL participated in the design of the study, wrote the study protocol. CD and NA participated in establishing the sample size and will help to recruit patients. MR set up statistical analysis plan and determine sample size. RT revised the manuscript, will include patients into the protocol and collect and analyse data. JLP designed the study, critically revised the manuscript, will include patients, and collect and analyse data. JCB designed the study, critically revised the manuscript and will analyse data. The submitted manuscript has been approved by all authors.

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Competing interests Mr. R. Merle is a recipient of a grant from Agir pour les Maladies

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Chroniques, <http://fonds-apmc.org/>. CD, NA, JCB are employees of *AGIR* à dom. CP and
JLP received grants from Agir pour les Maladies Chroniques, <http://fonds-apmc.org/>.

Ethics approval

The protocol to be approved by The French Regional Ethics Committee CPP Ouest II-
Angers.

Provenance and peer review: not commissioned; externally peer reviewed.

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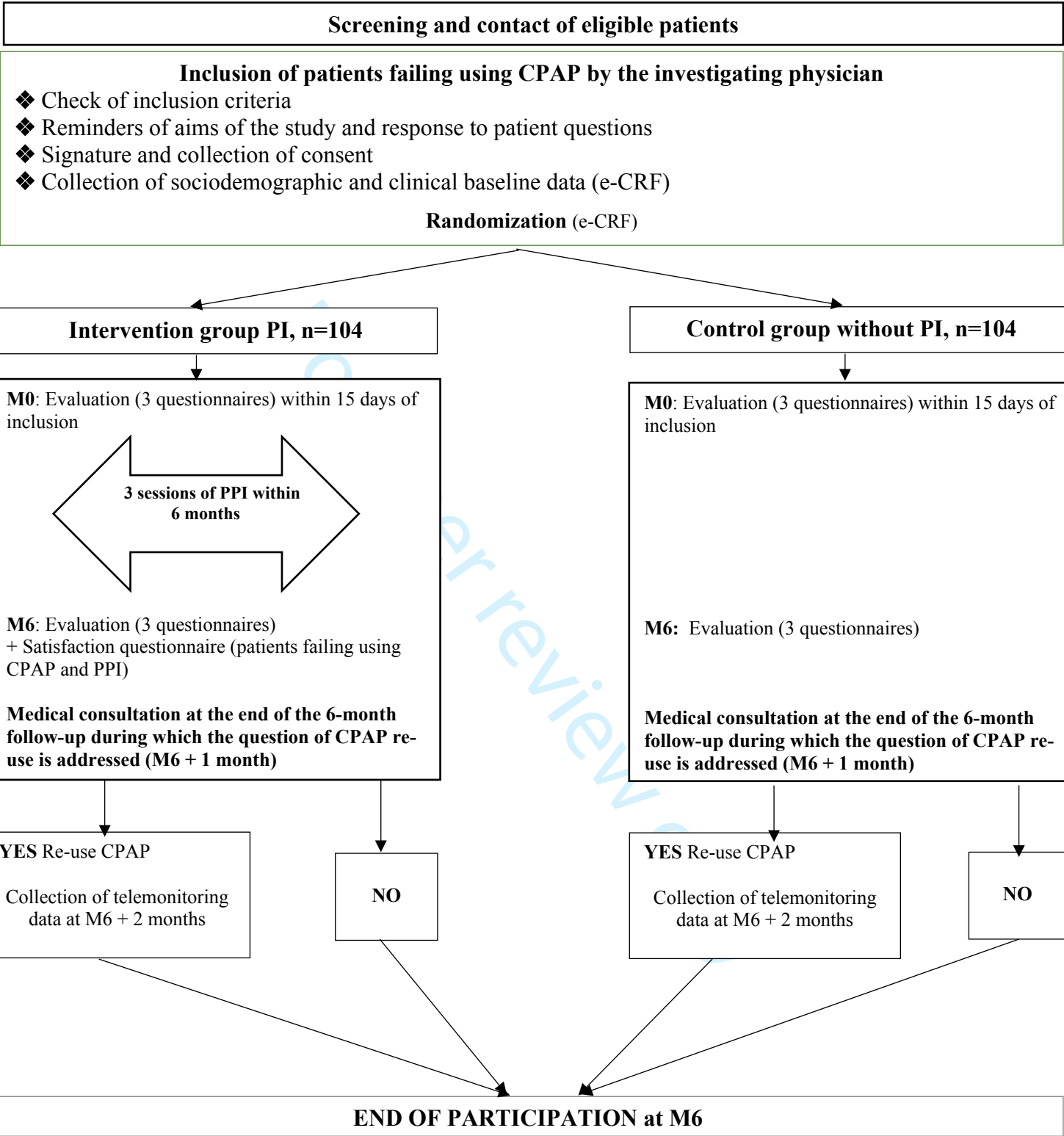
31-05-2021 version, *BMJ open Protocol***Table 1 -Inclusion and exclusion criteria**

| Inclusion criteria | Exclusion criteria |
|---|---|
| <ul style="list-style-type: none"> Over 18 years' old Diagnosed with of severe OSA (AHI \geq 30 events/hour) Discontinuation of CPAP 4 to 12 months after initiation and having stopped their CPAP treatment no later than one year prior to their inclusion Followed by the home health care provider AGIRaDom Access to a computer and/or tablet and an internet connection Oral and written French Able to provide written informed consent Affiliated to social security or beneficiary of such a scheme | <ul style="list-style-type: none"> CPAP cessation due to a resolution of the OSAS (e.g. weight loss after bariatric surgery) or another pathology that prevents the continuation of treatment (e.g. ENT surgery, etc.) Severe and/or unstable comorbidity that required hospitalisation for decompensation in the previous year (heart, kidney, respiratory, liver, psychiatric or other insufficiency) Central sleep apnoea index above 20% of AHI at the time of diagnosis Patient being treated with a mandibular advancement orthosis Lack of availability (e.g. night worker or patient who travels frequently, etc.). Current participation in, participation in the month prior to inclusion in another clinical intervention research study that may impact the study: this impact is left to the investigator's discretion. Referred to in Articles L1121-5 to L1121-8 of the CSP (corresponds to all protected persons: pregnant woman, breastfeeding mother, person deprived of liberty by judicial or administrative decision, person subject to a legal protection measure) |

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Figure 1, Work-flow



BMJ Open

A peer-driven intervention to help patients resume CPAP therapy following discontinuation: a multicenter, randomized clinical trial with patient involvement

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A peer-driven intervention to help patients resume CPAP therapy following discontinuation: a multicenter, randomized clinical trial with patient involvement

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27 **ABSTRACT**

28 **Introduction**

29 Obstructive Sleep Apnoea Syndrome (OSAS) is one of the most common chronic diseases.
30 It may be associated with symptoms of excessive daytime sleepiness and neurocognitive
31 and cardiovascular complications. First line therapy for OSAS involves home Continuous
32 Positive Airway Pressure (CPAP), however nearly half of patients do not adhere with this
33 treatment over the long-term. Cognitive-behavioural interventions that include health
34 professionals and patient and public involvement (PPI) are increasingly advocated in the
35 fields of education and research. We hypothesize that a peer-driven intervention could help
36 patients with OSAS to resume CPAP use after discontinuation.

37 **Methods and analysis**

38 We have designed a prospective, multicentre randomized, controlled trial that will be co-
39 conducted by health professionals, a home provider of CPAP and patients as experts or
40 peers or participants. The primary aim is to evaluate the impact of a 6-month, peer-driven
41 intervention to promote the resumption of CPAP after discontinuation. We anticipate that
42 20% of patients in the intervention group will reuse CPAP as compared to 6% in control
43 group, thus 104 patients must be included in each group. The secondary aims are i) to
44 evaluate the impact of the peer-driven intervention on adherence to CPAP compared to the
45 control group (mean adherence and percentage of nights with at least 4 hours' use /night
46 for 70% of nights); - ii) to determine factors associated with resumption of CPAP; -iii) to
47 assess patient satisfaction with the peer-driven intervention at 6 months; -iv) to evaluate
48 the feasibility and the execution of the peer-driven intervention and peer satisfaction. Adult
49 outpatients with an established diagnosis of severe OSA (Apnea-Hypopnea Index >30
50 events/hour) that have stopped using CPAP within 4 to 12 months after initiation will be
51 recruited. The peers who will perform the intervention will be patients with OSAS treated
52 with CPAP with good adherence (at least 4 hours/night, 70% of nights) and trained in

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motivational enhancement and cognitive-behavioural therapies. Trained peers will conduct 3 interviews within 6 months with participants.

Ethics and dissemination

Ethical approval has been obtained from the French Regional Ethics Committee CPP Ouest II-Angers, (IRB 21.02.25.68606 (2021/25)). All participants will sign written informed consent. The results will be presented at conferences and published in peer-reviewed journals as well as public media.

Trial registration number: NCT04538274

Strengths and limitations of this study

- Patient involvement (PI) from the beginning of the setup of this trial.
- There is a rationale supporting the use of motivational enhancement and cognitive-behavioural therapies performed by peers to promote CPAP resumption.
- Our team has experience in patient and public involvement (PPI) from work undertaken at the Grenoble Alpes University Department of Patients.
- Challenges are to train enough peers with homogenous skills.

Key words: patient and public involvement (PPI), obstructive sleep apnoea syndrome (OSAS), excessive daytime sleepiness, non-adherence, motivational enhancement and cognitive-behavioural therapies

Abbreviations and website addresses

AGIR à dom. Home care and services, Meylan, France, <https://www.agiradom.com/en/>

AHI Apnoea + Hypopnea Index

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| 1 | 31-05-2021 version, <i>BMJ open Protocol-R1</i> , revised document, the 4 th of August 2021 |
| 2 | |
| 3 | CPAP Continuous Positive Airway Pressure |
| 4 | |
| 5 | DUPGA Département Universitaire des Patients Grenoble Alpes: Grenoble Alpes University |
| 6 | |
| 7 | Department of Patients, https://medecine.univ-grenoble- |
| 8 | |
| 9 | alpes.fr/departements/departement-universitaire-des-patients/ |
| 10 | |
| 11 | EDS Excessive Daytime Sleepiness |
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| 14 | OSAS Obstructive Sleep Apnoea Syndrome |
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| 16 | PI Patient Involvement |
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| 18 | PPI Patient and Public Involvement |
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79 INTRODUCTION

80 Obstructive Sleep Apnoea syndrome (OSAS) is one of the most common chronic diseases.
81 It is characterized by recurrent episodes of upper airway collapse during sleep, and may or
82 may not be associated symptoms of excessive daytime sleepiness (EDS) and
83 neurocognitive and cardiovascular complications [1]. Twelve million adults aged between
84 30 and 69 years may have moderate to severe OSAS in France, based on an Apnoea
85 Hypopnea Index (AHI) threshold value of 15 or more events per hour of sleep [2]. The
86 risks associated with the disease can be severe, for example, individuals with untreated
87 OSAS have a three times greater risk of motor vehicle accidents than the general population
88 [3]. OSAS is also associated with an increased risk of cardiovascular disease, diabetes and
89 glucose dysregulation [4], independent from obesity [5].
90 The first line therapy for OSAS is continuous positive airway pressure (CPAP) [1,6,7].
91 CPAP has been shown to effectively reduce EDS and to improve daily functioning,
92 cognitive function, mood and quality of life [3,6]. The use of CPAP also reduces traffic
93 accidents [7] and other work-related injuries, and improves work productivity [8].
94 Although CPAP therapies are highly effective in normalizing AHI and reducing symptoms
95 in symptomatic patients, treatment success is limited by long term nonadherence in nearly
96 half of patients [9]. Technical progress in the systems and interfaces (soundproofing,
97 improved masks, humidification, pressure modulation, etc.) have unfortunately not been
98 sufficient to improve compliance [10,11]. Equally, the effect sizes of telemedicine
99 approaches are not as large as what has been achieved with the use of behavioural therapies,
100 and the impacts on patient and provider satisfaction and cost-effectiveness are not yet clear
101 [12–15].
102 Nonadherence is related to users' profiles, their representations of OSAS and the benefits
103 they experience from CPAP [12,16,17]. This is why cognitive-behavioural and
104 motivation enhancement therapies conducted by health professionals could be effective in

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ensuring adherence to CPAP. A Cochrane review in 2014 showed that there is a low level of evidence that such interventions increase CPAP use (by 1.44 h per night in six studies; n = 584) and increase the number of participants who used their devices for longer than four hours per night (from 28 to 47% in 3 studies; n= 358)[18]. More robust studies are thus needed to increase the level of evidence regarding these types of interventions.

In addition, patient and public involvement (PPI) is more and more advocated in the fields of health education and research [19–25]. Nevertheless, the efficacy of PPI remains to be demonstrated [26]. To our knowledge, only one previous pilot study in 39 patients showed that one-to-one peer support at CPAP initiation was feasible and generated high patient satisfaction. However, the study was not powerful enough to demonstrate effectiveness in terms of adherence to CPAP [18,27]. The data from the study, are, however, useful for designing further studies.

The aim of this adequately powered randomized clinical trial is therefore to assess the role of trained Patient Involvement (PI) representatives to help patients with OSAS to restart CPAP after discontinuation.

METHODS AND ANALYSIS

Study design

This is a prospective, multicentre, randomized controlled trial that will be co-conducted by health professionals, a CPAP home provider and patients as experts or peers or participants. After signing a consent form, patients' participants will be randomized 1:1 to the intervention group with peers or the control group. *Nota bene*: the peers involved in the conduct of the study will sign a confidentiality agreement of non-divulgence of the information exchanged with the participants.

Objectives

Primary research aim

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The primary aim is to evaluate the impact of a 6-month intervention involving trained PI representatives to promote the resumption of CPAP in patients who have discontinued its use. Resumption of CPAP is defined as the medical prescription and the setting up of a new CPAP device at home by the homecare provider.

Secondary research aims:

- i) to evaluate the impact of the peer-driven intervention on adherence to CPAP by comparing adherence with the control group (mean adherence and % of nights with at least 4 hours' use /night for 70 % of nights);
- ii) to determine the factors associated with the resumption of CPAP treatment;
- iii) to assess the satisfaction of the intervention group with the peer-driven intervention at 6 months;
- iv) to evaluate the feasibility and the execution of the peer-driven intervention and the satisfaction of peers after the interviews conducted.

Patients, Table 1

Adults with an established diagnosis of severe OSAS (AHI >30 events/hour) who have discontinued CPAP by returning their device to the homecare provider within 4 to 12 months after CPAP initiation will be recruited, Table 1, according to the study flow chart depicted in Figure 1.

Interventions (Figure 1)

Recruitment and training of PI representatives

PI representatives will be recruited from the investigators clinics. To be recruited as a PI representative, patients should:

- have used home CPAP for at least one year,
- have a CPAP adherence of at least 4 h/night for 70% of nights,

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157 - express their motivation in participating in a training and orientation session conducted
158 by research staff and including expert patients from the Grenoble Alpes University
159 Department of Patients (DUP GA) [28],

160 - accept to conduct 3 motivational sessions by videoconference meetings of 45 to 60
161 minutes duration with 5 to 8 patients within 6 months after each patient's inclusion,

162 Patients with any major psychiatric illness, shift-workers or frequent out of town travellers
163 will not be recruited as peers.

164 Peers will be trained during a three half-days interactive session organised by DUP GA,
165 with experts in patient therapeutic education and communication, and investigators [28].

166 Peers will be taught how to interact with the patients recruited in the study: the aim is for
167 them to share their experiences but not to provide any medical advice.

168 *Description of the intervention*

169 Trained peers will meet patients randomized into the intervention group by
170 videoconference. Each PI representative will be allocated 5 to 8 patients. They will conduct
171 3 face to face motivational sessions, each of 45 to 60 minutes duration, over a 6-month
172 period based on the principle of motivational enhancement and cognitive-behavioural
173 therapies [11,13]. The content of the first session is designed to identify and understand the
174 underlying reasons for stopping CPAP treatment and to identify difficulties encountered
175 by the patient (advantages and disadvantages of CPAP treatment). The aim of the second
176 session will be for the patient to define his/her objectives and priorities. During the last
177 session, will be discussed to strengthen the motivation to change and how to plan for it.
178 The peers will receive 100 € per patient for the 3 interviews.

179 In the control group, patients will be informed, at inclusion, that they can have a visit with
180 a physician investigator at any time to resume treatment if they wish, as is usual practice.

181 At the end of the six-month follow-up period, all patients in both groups will have a
182 consultation with their physician who will suggest they resume CPAP treatment. This visit

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may take place earlier if the patient wishes to resume CPAP treatment before the end of the follow-up period. We planned to start inclusions by November 2021 and end the study by December 2023.

Assessment in blinded manner at months 0 and 6

Average adherence to CPAP will be measured from data recorded by the built-in software of the CPAP devices (via tele monitoring or retrieved by a home technician) for 1 month after the final consultation.

The relationship between the variables below and a positive response to the peers intervention (defined by a restart of CPAP treatment) will be analyzed: age, sex, Body Mass Index (BMI), marital status, education level, socio-professional status, precariousness (using the EPICES score), smoking and alcohol use, comorbidities (using Charlson score), history of OSAS (date of diagnosis of OSAS, baseline AHI), observance to treatments (Girerd score), date and reason for stopping CPAP and EDS score (using the Epworth Sleepiness Scale).

To determine patient profiles, their representations of OSAS, their experiences with CPAP and their knowledge and confidence to manage their health, 3 questionnaires will be completed at inclusion (M0) and at the 6-month follow-up (M6): the Functional Outcomes of Sleep Questionnaire (FOSQ) a disease-specific quality of life questionnaire [29], the Patient Activation Measure (PAM) a measure that assesses patient knowledge, skill, and confidence for self-management [30] and the Self-Efficacy Measure for Sleep Apnea (SEMSA) [31,32] a tool with strong psychometric properties that identifies patient perceptions that may indicate those most likely not to adhere to treatment.

The satisfaction of participating patients with the PI intervention and the satisfaction of PI representatives will be measured on a 4-point Likert scale: very dissatisfied, dissatisfied, satisfied, very satisfied.

Finally, the feasibility and the execution of the 3 interviews will be assessed by the

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number of interviews carried out in their entirety and the average duration of each interview (in minutes).

All information will be collected in secure electronic medical records in accordance with the requirements of General Data Protection Regulation.

Statistical analysis

Sample size

We hypothesize that 20% of patients allocated to the intervention group will reuse CPAP 6 months as compared to 6% of patients in the control group. A two group χ^2 test with a 5% two-sided significance level will have 80% power to detect such difference between the two groups when the sample size in each group is 90 (nQuery v8, Statistical Solutions, Cork, Ireland). In order to take into account a possible drop-outs and to comply with the intent-to-treat principle, we will inflate the sample size by a factor of 15% [33]. We thus plan to include 104 patients per group (i.e. 208 patients in total). 15 patient peers will be involved.

Feasibility and recruitment

The home care provider, *AGIR à dom.* follows more than 20,000 patients with OSAS who use CPAP in the south of France. In 2018, out of 3,281 patients who started CPAP within the study area (Isère, Savoie and Haute-Savoie), 365 discontinued it between 4 to 12 months post initiation and 6% resumed use within 6 months after discontinuation.

Randomization

After consent, randomization will be performed by a centralized computer software for each investigating center. It will be stratified on the center.

Statistical analysis plan

Descriptive analyses: continuous variables will be expressed as medians (25th/75th percentiles) or means (SD) depending on normality which will be assessed with the Shapiro-Wilk test. Categorical variables will be reported as absolute numbers and

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percentages for both groups. Baseline comparisons between groups will be made using a Student's t-test or Mann-Whitney U test, depending on the distribution. For discrete variables, a χ^2 test will be used. If significant differences are observed between arms, ANOVA and multivariable regression will be performed. In the case of missing data, an imputation strategy will be applied according to the percentage of missing values. Data management and statistical analyses will be performed using SAS, V.9.4, SAS Institute.

Primary outcome analysis: the impact of the PI intervention on the resumption of CPAP treatment will be studied by comparing the resumption of CPAP in the 2 arms, using a Chi-square test. To take into account a possible centre effect, a second analysis will be carried out using a conditional logistic regression stratified by the centre; the intervention or control arm will be considered as the dependent variable.

Secondary outcomes analyses: mean CPAP compliance one month after resumption of CPAP will be analysed using a mixed linear model (fixed factor: randomisation arm (intervention vs. control), random factor: centre). Comparison of the probability of resuming CPAP with an average compliance of at least 4 hours/night, 70% of nights between the intervention and control groups will be analysed using a conditional logistic regression, stratified by centre. All analyses will be performed as intention-to-treat and then a sensitivity analysis will also be performed *per protocol* (patients who have not resumed treatment will be considered to have zero adherence).

The association between resumption of CPAP and the sociodemographic parameters, clinical data and the scores of the three questionnaires will be studied by conditional logistic regression models stratified by centre, and adjusted by arm (intervention vs control).

In the intervention arm, descriptive statistics will be presented on the satisfaction as well as on the number of interviews carried out and their average duration.

Ethics

The study will be conducted in accordance with the Declaration of Helsinki and the recommendations for Good Clinical Practice. Written informed consent will be signed by all study participants before enrolment in the study. Patients will have the right to withdraw from the study without incurring any prejudice at any time.

Patient involvement

RM, first author and expert patient, and members of DUP GA participated in the design of this study and will participate in all stages including teaching peers [28] and promoting and reporting the data, including publication in peer review. Thanks to training with health professionals and expert patients [22,23,25] peers will adopt the appropriate posture to enable patients to find their own resources to overcome barriers to use CPAP.

Dissemination

Dissemination plans of the results include presentations at conferences and a publication in peer-reviewed journal. Updates of the randomized trial will be available at ClinicalTrials.gov. All patients will be informed that the dissemination of results will be accessible on request.

Sponsor and funding

The study sponsor will be AGIR à dom. Co-Principal investigators are RM, an expert patient, and JCB, a researcher. The collaborators and sponsors were not involved in the design of the study and will not influence the execution, analysis or publication of results.

DISCUSSION

OSAS is associated with many negative health consequences [1]. The lack of compliance with home CPAP therapy, which is the first line of treatment, and which has shown to be effective on quality of life is a major issue both in terms of the patient's own health status and in health care utilisation [1,2,7,8]. Attempts have been made to improve CPAP

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compliance by improving technical issues relating to the comfort of use of the system [10,11] and the use of the of remote monitoring and telemedicine, along with the implementation of web-based adherence interventions [12–15]; however they have not been shown to improve compliance with the therapy. Other strategies to improve compliance therefore need to be developed and tested.

One of the main strengths of this study is the involvement of peers in the implementation of the behavioural intervention. Regarding efficacy, the involvement of patients with experience in the motivation of their peers to comply with treatment has been implemented with success in other chronic conditions requiring self-management such as HIV and diabetes [34,35]. Furthermore, evidence suggests that patients perceive peers with similar comorbidities as more credible than health-care professionals in the delivery of behavioural interventions [36–38]. The concept of PPI in education and research has been adopted by a growing number of medical schools, particularly in the United kingdom [19,24]. If the results of this study confirm the effectiveness of the PI intervention in promoting resumption of CPAP in patients initially failing CPAP, this study will provide an evidence base to support the use of PI in the management of OSAS in conjunction with the home healthcare provider and specialized sleep centers [39].

The aim to seek factors that are related to CPAP resumption will provide useful information regarding those patients who are more likely to resume CPAP and therefore who PI interventions are more likely to help. This will open the way for further studies to determine the most appropriate methods to improve compliance in those patients who benefit less from PI interventions.

Despite these strengths, the study has two main inherent limitations. Firstly, the results are likely to be biased by the fact that patients who accept to participate may be more likely to resume CPAP therapy than those who decline participation. The results may therefore not be generalizable to all patients who have stopped using their CPAP as prescribed.

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Secondly, the effectiveness of the intervention may also depend on the capacity of the peer-participant to deliver it. The training is quite short (3 half-days) and some of the peers recruited may be more skilled than others in providing such intervention. However, in this study, the peers will be additionally supported throughout the study by the University Department of Patients.

In summary, the results of this study will determine the effectiveness of a PI intervention to motivate patients who have stopped using their CPAP as prescribed to resume its use on compliance with CPAP therapy. The results will also provide information regarding the factors relating to resumption of CPAP, providing a starting point for further studies to determine the most appropriate methods to improve compliance in those patients who benefit less from PI interventions.

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Contributors RM participated in the design of the study, wrote the article based on the study protocol, will train PI, collect and analyse data into the protocol. CP participated in the design of the study, wrote the study protocol and will include patients into the protocol together with PPI. SL participated in the design of the study, wrote the study protocol. CD and NA participated in establishing the sample size and will help to recruit patients. MR set up statistical analysis plan and determine sample size. RT revised the manuscript, will include patients into the protocol and collect and analyse data. JLP designed the study, critically revised the manuscript, will include patients, and collect and analyse data. JCB designed the study, critically revised the manuscript and will analyse data. The submitted manuscript has been approved by all authors.

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Competing interests Mr. R. Merle is a recipient of a grant from Agir pour les Maladies

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3 354 Chroniques, <http://fonds-apmc.org/>. CD, NA, JCB are employees of *AGIR* à dom. CP and
4
5 355 JLP received grants from Agir pour les Maladies Chroniques, <http://fonds-apmc.org/>.
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9 357 **Ethics approval**
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11 358 The protocol to be approved by The French Regional Ethics Committee CPP Ouest II-
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18 361 **Provenance and peer review:** not commissioned; externally peer reviewed.
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23 363 **Open access** This is an open access article distributed in accordance with the Creative
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30 366 derivative works on different terms, provided the original work is properly cited,
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Table 1 -Inclusion and exclusion criteria

| Inclusion criteria | Exclusion criteria |
|--|---|
| <ul style="list-style-type: none"> Over 18 years' old Diagnosed with of severe OSA (AHI \geq 30 events/hour) Discontinuation of CPAP 4 to 12 months after initiation, despite the interventions of health professionals and provider, and having stopped their CPAP treatment no later than one year prior to their inclusion Followed by the home health care provider AGIRaDom Access to a computer and/or tablet and an internet connection Oral and written French Able to provide written informed consent Affiliated to social security or beneficiary of such a scheme | <ul style="list-style-type: none"> CPAP cessation due to a resolution of the OSAS (e.g. weight loss after bariatric surgery) or another pathology that prevents the continuation of treatment (e.g. ENT surgery, etc.) Severe and/or unstable comorbidity that required hospitalization for decompensation in the previous year (heart, kidney, respiratory, liver, psychiatric or other insufficiency) Central sleep apnoea index above 20% of AHI at the time of diagnosis Patient being treated with a mandibular advancement orthosis Lack of availability (e.g. night worker or patient who travels frequently, etc.). Current participation in, participation in the month prior to inclusion in another clinical intervention research study that may impact the study: this impact is left to the investigator's discretion. Referred to in Articles L1121-5 to L1121-8 of the CSP (corresponds to all protected persons: pregnant woman, breastfeeding mother, person deprived of liberty by judicial or administrative decision, person subject to a legal protection measure) |

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499 **Figure 1. Study design**

501 **Supplementary file**
502 SPIRIT 2013 Checklist

| Section/item | ItemNo, ligne manuscrit | Description |
|--------------------------------------|--|--|
| Administrative information | | |
| Title | 1, 1-2 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym |
| Trial registration | 2a, 62 | Trial identifier and registry name. If not yet registered, name of intended registry |
| 2b, | All items from the World Health Organization Trial Registration Data Set | |
| Protocol version | 3, joined, 6-05-2021, v1.1 | Date and version identifier |
| Funding | 4, 284-6 | Sources and types of financial, material, and other support |
| Roles and responsibilities | 5a, 340-9 | Names, affiliations, and roles of protocol contributors |
| 5b, C. Pison, cpison@chu-grenoble.fr | Name and contact information for the trial sponsor | |
| 5c, none | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | |
| 5d, PI as C. Pison | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | |
| Introduction | | |
| Background and rationale | 6a, 86-124 | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention |
| 6b Objectives | 7, 135-149 | Explanation for choice of comparators Specific objectives or hypotheses |

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| | | |
|---|--------------|---|
| Trial design | 8, Fig. 1 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) |
| Methods: Participants, interventions, and outcomes | | |
| Study setting | 9, 152-5 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained |
| Eligibility criteria | 10, Table 1 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) |
| Interventions | 11a, 157-191 | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered |
| 11b, NA | | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) |
| 11c, Fig. 1 | | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) |
| 11d, none | | Relevant concomitant care and interventions that are permitted or prohibited during the trial |
| Outcomes | 12, 136-149 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy |

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|--|----------------------------------|--|
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| | | and harm outcomes is strongly recommended |
| Participant timeline | 13, Fig. 1 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) |
| Sample size | 14, 220-8 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations |
| Recruitment | 15, 229-33 | Strategies for achieving adequate participant enrolment to reach target sample size |
| Methods: Assignment of interventions (for controlled trials) | | |
| Allocation: | | |
| Sequence generation | 16a, 235-6 | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions |
| Allocation concealment mechanism | 16b, 235-6 | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned |
| Implementation | 16c, 235-6 | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions |
| Blinding (masking) | 17a, NA except outcome assessors | Who will be blinded after assignment to interventions (eg, trial participants, care |

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17b, NA providers, outcome assessors, data analysts), and how
If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial

Methods: Data collection, management, and analysis

Data collection methods 18a Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

18b, 229-233 Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

Data management 19, see Protocol Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol

Statistical methods 20a, 237-265 Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol

20b, NA Methods for any additional analyses (eg, subgroup and adjusted analyses)

20c, NA Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

Methods: Monitoring

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| Data monitoring | 21a, monitoring independant from investigators | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed |
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| 21b, NA | | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial |
| Harms, NA | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct |
| Auditing | 23 every 3 months | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor |
| Ethics and dissemination | | |
| Research ethics approval | 24, 267-271 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval |
| Protocol amendments | 25, investigators | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) |
| Consent or assent | 26a, patient's doctor | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) |
| 26b, NA | | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable |
| Confidentiality | 27, | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial |
| Declaration of interests | 28, 359-61 | Financial and other competing interests for principal investigators for the overall trial and each study site |
| Access to data | 29, investigators | Statement of who will have access to the final trial dataset, and disclosure of |

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| | | contractual agreements that limit such access for investigators |
| Ancillary and post-trial care | 30, NA | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation |
| Dissemination policy | 31a, 279-82 | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions |
| 31b | | Authorship eligibility guidelines and any intended use of professional writers |
| 31c | | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code |
| Appendices | | |
| Informed consent materials | 32, protocol | Model consent form and other related documentation given to participants and authorised surrogates |
| Biological specimens | 33, NA | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable |

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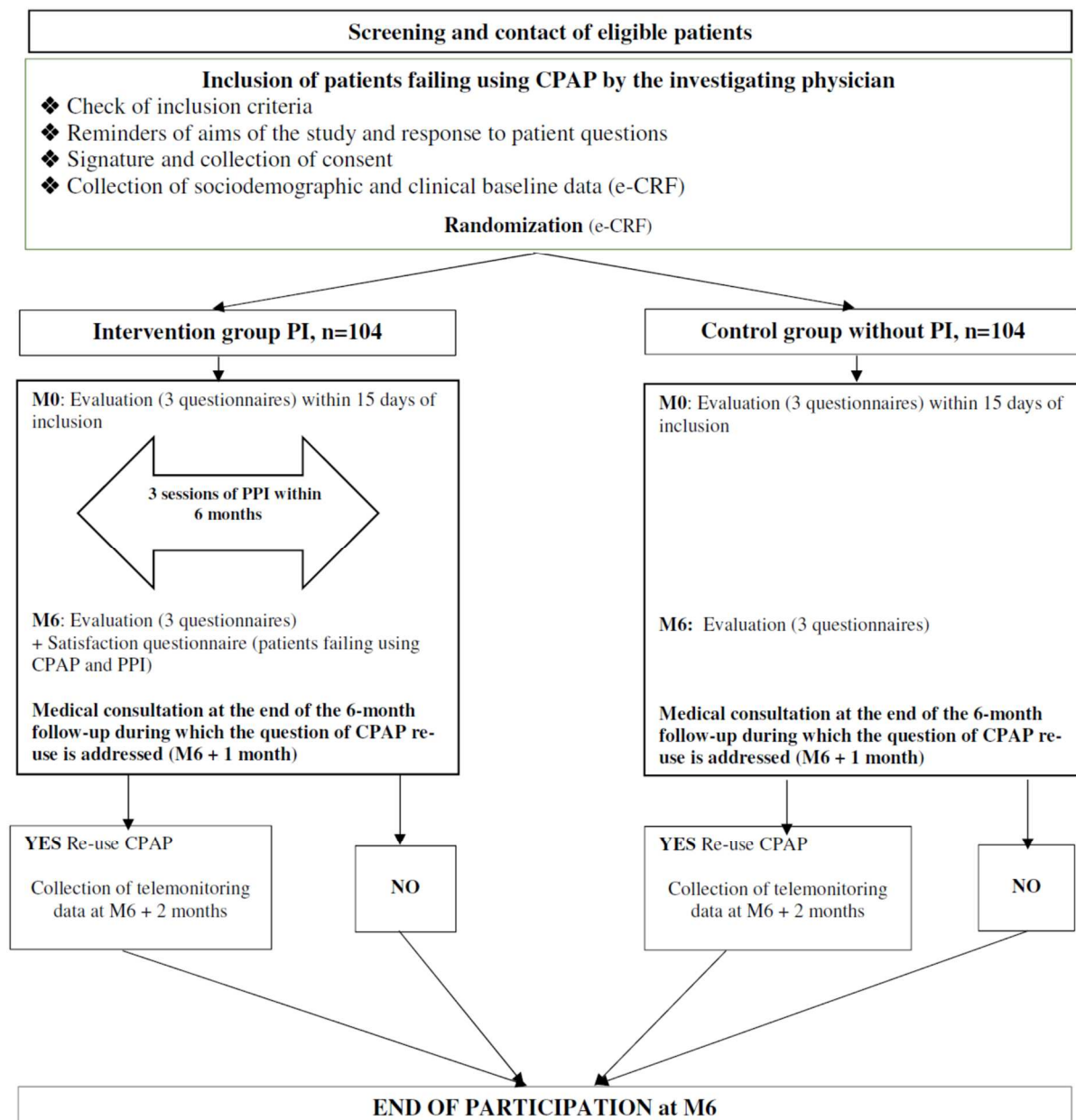
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Figure 1, Work-flow



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SPIRIT 2013 Checklist

| Section/item | ItemNo, ligne manuscript | Description |
|--------------------------------------|----------------------------|--|
| Administrative information | | |
| Title | 1, 1-2 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym |
| Trial registration | 2a, 62 | Trial identifier and registry name. If not yet registered, name of intended registry |
| 2b, | | All items from the World Health Organization Trial Registration Data Set |
| Protocol version | 3, joined, 6-05-2021, v1.1 | Date and version identifier |
| Funding | 4, 284-6 | Sources and types of financial, material, and other support |
| Roles and responsibilities | 5a, 340-9 | Names, affiliations, and roles of protocol contributors |
| 5b, C. Pison, cpison@chu-grenoble.fr | | Name and contact information for the trial sponsor |
| 5c, none | | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities |
| 5d, PI as C. Pison | | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) |
| Introduction | | |
| Background and rationale | 6a, 86-124 | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention |
| 6b | | Explanation for choice of comparators |
| Objectives | 7, 135-149 | Specific objectives or hypotheses |
| Trial design | 8, Fig. 1 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, |

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| | | equivalence, noninferiority, exploratory) |
| Methods: Participants, interventions, and outcomes | | |
| Study setting | 9, 152-5 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained |
| Eligibility criteria | 10, Table 1 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) |
| Interventions | 11a, 157-191 | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered |
| 11b, NA | | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) |
| 11c, Fig. 1 | | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) |
| 11d, none | | Relevant concomitant care and interventions that are permitted or prohibited during the trial |
| Outcomes | 12, 136-149 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended |
| Participant timeline | 13, Fig. 1 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic |

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| | | diagram is highly recommended (see Figure) |
| Sample size | 14, 220-8 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations |
| Recruitment | 15, 229-33 | Strategies for achieving adequate participant enrolment to reach target sample size |
| Methods: Assignment of interventions (for controlled trials) | | |
| Allocation: | | |
| Sequence generation | 16a, 235-6 | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions |
| Allocation concealment mechanism | 16b, 235-6 | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned |
| Implementation | 16c, 235-6 | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions |
| Blinding (masking) | 17a, NA except outcome assessors | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how |
| 17b, NA | | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial |
| Methods: Data collection, management, and analysis | | |

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| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol |
| 18b, 229-233 | | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols |
| Data management | 19, see Protocol | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol |
| Statistical methods | 20a, 237-265 | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol |
| 20b, NA | | Methods for any additional analyses (eg, subgroup and adjusted analyses) |
| 20c, NA | | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) |
| Methods: Monitoring | | |
| Data monitoring | 21a, monitoring independent from investigators | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further |

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details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

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| Ethics and dissemination | | |
| Research ethics approval | 24, 267-271 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval |
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| Access to data | 29, investigators | Statement of who will have access to the final trial dataset, and disclosure of |

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| 11 | Dissemination policy | 31a, 279-82 |
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| 31 | Appendices | |
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BMJ Open

A peer-driven intervention to help patients resume CPAP therapy following discontinuation: a multicenter, randomized clinical trial with patient involvement

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| Manuscript ID | bmjopen-2021-053996.R2 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 26-Sep-2021 |
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| Keywords: | RESPIRATORY MEDICINE (see Thoracic Medicine), SLEEP MEDICINE, Chronic airways disease < THORACIC MEDICINE |
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A peer-driven intervention to help patients resume CPAP therapy following discontinuation: a multicenter, randomized clinical trial with patient involvement

Raymond Merle^{1,2,3}, Christophe Pison¹⁻⁴, Sophie Logerot^{5,6}, Chrystèle Deschaux^{5,6}, Nathalie Arnol^{5,6}, Matthieu Roustit^{1,7,8}, Renaud Tamisier^{1,8,9}, Jean Louis Pepin^{1,4,8*}, Jean Christian Borel^{5,6,8*}

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27 **ABSTRACT**

28 **Introduction**

29 Obstructive Sleep Apnoea Syndrome (OSAS) is one of the most common chronic diseases.
30 It may be associated with symptoms of excessive daytime sleepiness and neurocognitive
31 and cardiovascular complications. First line therapy for OSAS involves home Continuous
32 Positive Airway Pressure (CPAP), however nearly half of patients do not adhere with this
33 treatment over the long-term. Cognitive-behavioural interventions that include health
34 professionals and patient and public involvement (PPI) are increasingly advocated in the
35 fields of education and research. We hypothesize that a peer-driven intervention could help
36 patients with OSAS to resume CPAP use after discontinuation.

37 **Methods and analysis**

38 We have designed a prospective, multicentre randomized, controlled trial that will be co-
39 conducted by health professionals, a home provider of CPAP and patients as experts or
40 peers or participants. The primary aim is to evaluate the impact of a 6-month, peer-driven
41 intervention to promote the resumption of CPAP after discontinuation. We anticipate that
42 20% of patients in the intervention group will reuse CPAP as compared to 6% in control
43 group, thus 104 patients must be included in each group. The secondary aims are i) to
44 evaluate the impact of the peer-driven intervention on adherence to CPAP compared to the
45 control group (mean adherence and percentage of nights with at least 4 hours' use /night
46 for 70% of nights); - ii) to determine factors associated with resumption of CPAP; -iii) to
47 assess patient satisfaction with the peer-driven intervention at 6 months; -iv) to evaluate
48 the feasibility and the execution of the peer-driven intervention and peer satisfaction. Adult
49 outpatients with an established diagnosis of severe OSA (Apnea-Hypopnea Index >30
50 events/hour) that have stopped using CPAP within 4 to 12 months after initiation will be

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recruited. The peers who will perform the intervention will be patients with OSAS treated with CPAP with good adherence (at least 4 hours/night, 70% of nights) and trained in motivational enhancement and cognitive-behavioural therapies. Trained peers will conduct 3 interviews within 6 months with participants.

Ethics and dissemination

Ethical approval has been obtained from the French Regional Ethics Committee CPP Ouest II-Angers, (IRB 21.02.25.68606 (2021/25)). All participants will sign written informed consent. The results will be presented at conferences and published in peer-reviewed journals as well as public media.

Trial registration number: NCT04538274

Strengths and limitations of this study

- Patient involvement (PI) from the beginning of the setup of this trial.
- There is a rationale supporting the use of motivational enhancement and cognitive-behavioural therapies performed by peers to promote CPAP resumption.
- Our team has experience in patient and public involvement (PPI) from work undertaken at the Grenoble Alpes University Department of Patients.
- Challenges are to train enough peers with homogenous skills.

Key words: patient and public involvement (PPI), obstructive sleep apnoea syndrome (OSAS), excessive daytime sleepiness, non-adherence, motivational enhancement and cognitive-behavioural therapies

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76 **Abbreviations and website addresses**

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|-------------|---|
| AGIR à dom. | Home care and services, Meylan, France, https://www.agiradom.com |
| AHI | Apnoea + Hypopnea Index |
| CPAP | Continuous Positive Airway Pressure |
| DUPGA | Département Universitaire des Patients Grenoble Alpes: Grenoble Alpes University Department of Patients, https://medecine.univ-grenoble-alpes.fr/departements/departement-universitaire-des-patients/ |
| EDS | Excessive Daytime Sleepiness |
| OSAS | Obstructive Sleep Apnoea Syndrome |
| PI | Patient Involvement |
| PPI | Patient and Public Involvement |

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INTRODUCTION

Obstructive Sleep Apnoea syndrome (OSAS) is one of the most common chronic diseases.

It is characterized by recurrent episodes of upper airway collapse during sleep, and may or may not be associated symptoms of excessive daytime sleepiness (EDS) and neurocognitive and cardiovascular complications [1]. Twelve million adults aged between 30 and 69 years may have moderate to severe OSAS in France, based on an Apnoea Hypopnea Index (AHI) threshold value of 15 or more events per hour of sleep [2]. The risks associated with the disease can be severe, for example, individuals with untreated OSAS have a three times greater risk of motor vehicle accidents than the general population [3]. OSAS is also associated with an increased risk of cardiovascular disease, diabetes and glucose dysregulation [4], independent from obesity [5].

The first line therapy for OSAS is continuous positive airway pressure (CPAP) [1,6,7]. CPAP has been shown to effectively reduce EDS and to improve daily functioning, cognitive function, mood and quality of life [3,6]. The use of CPAP also reduces traffic accidents [7] and other work-related injuries, and improves work productivity [8]. Although CPAP therapies are highly effective in normalizing AHI and reducing symptoms in symptomatic patients, treatment success is limited by long term nonadherence in nearly half of patients [9]. Technical progress in the systems and interfaces (soundproofing, improved masks, humidification, pressure modulation, etc.) have unfortunately not been sufficient to improve compliance [10,11]. Equally, the effect sizes of telemedicine approaches are not as large as what has been achieved with the use of behavioural therapies, and the impacts on patient and provider satisfaction and cost-effectiveness are not yet clear [12–15].

Nonadherence is related to users' profiles, their representations of OSAS and the benefits they experience from CPAP [12,16,17]. This is why cognitive-behavioural and

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motivation enhancement therapies conducted by health professionals could be effective in ensuring adherence to CPAP. A Cochrane review in 2014 showed that there is a low level of evidence that such interventions increase CPAP use (by 1.44 h per night in six studies; n = 584) and increase the number of participants who used their devices for longer than four hours per night (from 28 to 47% in 3 studies; n= 358)[18]. More robust studies are thus needed to increase the level of evidence regarding these types of interventions.

In addition, patient and public involvement (PPI) is more and more advocated in the fields of health education and research [19–25]. Nevertheless, the efficacy of PPI remains to be demonstrated [26]. To our knowledge, only one previous pilot study in 39 patients showed that one-to-one peer support at CPAP initiation was feasible and generated high patient satisfaction. However, the study was not powerful enough to demonstrate effectiveness in terms of adherence to CPAP [18,27]. The data from the study, are, however, useful for designing further studies.

The aim of this adequately powered randomized clinical trial is therefore to assess the role of trained Patient Involvement (PI) representatives to help patients with OSAS to restart CPAP after discontinuation.

METHODS AND ANALYSIS

Study design

This is a prospective, multicentre, randomized controlled trial that will be co-conducted by health professionals, a CPAP home provider and patients as experts or peers or participants. After signing a consent form, patients’ participants will be randomized 1:1 to the intervention group with peers or the control group. *Nota bene:* the peers involved in the conduct of the study will sign a confidentiality agreement of non-divulgence of the information exchanged with the participants.

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Objectives

Primary research aim

The primary aim is to evaluate the impact of a 6-month intervention involving trained PI representatives to promote the resumption of CPAP in patients who have discontinued its use.

Primary research outcome

Resumption of CPAP is defined as the medical prescription and the setting up of a new CPAP device at home by the homecare provider.

Secondary research aims:

- i) to evaluate the impact of the peer-driven intervention on adherence to CPAP by comparing adherence with the control group (mean adherence and % of nights with at least 4 hours' use /night for 70 % of nights);
- ii) to determine the factors associated with the resumption of CPAP treatment;
- iii) to assess the satisfaction of the intervention group with the peer-driven intervention at 6 months;
- iv) to evaluate the feasibility and the execution of the peer-driven intervention and the satisfaction of peers after the interviews conducted.

Secondary research outcomes

- i. average adherence to CPAP will be measured from data recorded by the built-in software of the CPAP devices (via tele monitoring or retrieved by a home technician) for 1 month after the final consultation.
- ii. the relationship between the variables below and a positive response to the peers intervention (defined by a restart of CPAP treatment) will be analyzed: age, gender, Body Mass Index (BMI), marital status and number of young children (<10 years) education level, socio-professional status, fragility and social precariousness (using the

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EPICES score), smoking and alcohol use, comorbidities (using Charlson score), history of OSAS (date of diagnosis of OSAS, baseline AHI), observance to treatments (Girerd score), date and reason for stopping CPAP and EDS score (using the Epworth Sleepiness Scale). To determine patient profiles, their representations of OSAS, their experiences with CPAP and their knowledge and confidence to manage their health, 3 questionnaires will be completed at inclusion (M0) and at the 6-month follow-up (M6): the Functional Outcomes of Sleep Questionnaire (FOSQ) a disease-specific quality of life questionnaire [28], the Patient Activation Measure (PAM) a measure that assesses patient knowledge, skill, and confidence for self-management [29] and the Self-Efficacy Measure for Sleep Apnea (SEMSA) [30,31] a tool with strong psychometric properties that identifies patient perceptions that may indicate those most likely not to adhere to treatment.

iii. the satisfaction of participating patients with the PI intervention and the satisfaction of PI representatives will be measured on a 4-point Likert scale: very dissatisfied, dissatisfied, satisfied, very satisfied.

iv. the feasibility and the execution of the 3 interviews will be assessed by the number of interviews carried out in their entirety and the average duration of each interview (in minutes).

All information will be collected in secure electronic medical records in accordance with the requirements of General Data Protection Regulation.

Patients, Table 1

Adults with an established diagnosis of severe OSAS (AHI >30 events/hour) who have discontinued CPAP by returning their device to the homecare provider within 4 to 12 months after CPAP initiation will be recruited according to the study flow chart depicted

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in Figure 1.

Interventions (Figure 1)

Recruitment and training of PI representatives

PI representatives will be recruited from the investigators clinics. To be recruited as a PI representative, patients should, Table I:

- have used home CPAP for at least one year,
- have a CPAP adherence of at least 4 h/night for 70% of nights,
- express their motivation in participating in a training and orientation session conducted by research staff and including expert patients from the Grenoble Alpes University Department of Patients (DUP GA) [23],
- accept to conduct 3 motivational sessions by videoconference meetings of 45 to 60 minutes duration with 5 to 8 patients within 6 months after each patient's inclusion,

Patients with any major psychiatric illness, shift-workers or frequent out of town travellers will not be recruited as peers.

Peers will be trained during a three half-days interactive session organised by DUP GA, with experts in patient therapeutic education and communication, and investigators [23]. Peers will be taught how to interact with the patients recruited in the study: the aim is for them to share their experiences but not to provide any medical advice.

Description of the intervention

Trained peers will meet patients randomized into the intervention group by videoconference. Each PI representative will be allocated 5 to 8 patients. They will conduct 3 face to face motivational sessions, each of 45 to 60 minutes duration, over a 6-month period based on the principle of motivational enhancement and cognitive-behavioural therapies [11,13]. The content of the first session is designed to identify and understand the

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underlying reasons for stopping CPAP treatment and to identify difficulties encountered by the patient (advantages and disadvantages of CPAP treatment). The aim of the second session will be for the patient to define his/her objectives and priorities. During the last session, will be discussed to strengthen the motivation to change and how to plan for it.

The peers will receive 100 € per patient for the 3 interviews.

In the control group, patients will be informed, at inclusion, that they can have a visit with a physician investigator at any time to resume treatment if they wish, as is usual practice.

At the end of the six-month follow-up period, all patients in both groups will have a consultation with their physician who will suggest they resume CPAP treatment. This visit may take place earlier if the patient wishes to resume CPAP treatment before the end of the follow-up period. We planned to start inclusions by November 2021 and end the study by December 2023.

Statistical analysis

Sample size

We hypothesize that 20% of patients allocated to the intervention group will reuse CPAP 6 months as compared to 6% of patients in the control group. A two group χ^2 test with a 5% two-sided significance level will have 80% power to detect such difference between the two groups when the sample size in each group is 90 (nQuery v8, Statistical Solutions, Cork, Ireland). In order to take into account a possible drop-outs and to comply with the intent-to-treat principle, we will inflate the sample size by a factor of 15% [32].

We thus plan to include 104 patients per group (i.e. 208 patients in total). 15 patient peers will be involved.

Feasibility and recruitment

The home care provider, *AGIR à dom.* follows more than 20,000 patients with OSAS who use CPAP in the south of France. In 2018, out of 3,281 patients who started CPAP

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within the study area (Isère, Savoie and Haute-Savoie), 365 discontinued it between 4 to 12 months post initiation and 6% resumed use within 6 months after discontinuation.

Randomization

After consent, randomization will be performed by a centralized computer software for each investigating center. It will be stratified on the center.

Statistical analysis plan

Descriptive analyses: continuous variables will be expressed as medians (25th/75th percentiles) or means (SD) depending on normality which will be assessed with the Shapiro-Wilk test. Categorical variables will be reported as absolute numbers and percentages for both groups. Baseline comparisons between groups will be made using a Student's t-test or Mann-Whitney U test, depending on the distribution. For discrete variables, a χ^2 test will be used. If significant differences are observed between arms, ANOVA and multivariable regression will be performed. In the case of missing data, an imputation strategy will be applied according to the percentage of missing values. Data management and statistical analyses will be performed using SAS, V.9.4, SAS Institute.

Primary outcome analysis: the impact of the PI intervention on the resumption of CPAP treatment will be studied by comparing the resumption of CPAP in the 2 arms, using a Chi-square test. To take into account a possible centre effect, a second analysis will be carried out using a conditional logistic regression stratified by the centre; the intervention or control arm will be considered as the dependent variable.

Secondary outcomes analyses: mean CPAP compliance one month after resumption of CPAP will be analysed using a mixed linear model (fixed factor: randomisation arm (intervention vs. control), random factor: centre). Comparison of the probability of resuming CPAP with an average compliance of at least 4 hours/night, 70% of nights between the intervention and control groups will be analysed using a conditional logistic

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regression, stratified by centre. All analyses will be performed as intention-to-treat and then a sensitivity analysis will also be performed *per protocol* (patients who have not resumed treatment will be considered to have zero adherence).

The association between resumption of CPAP and the sociodemographic parameters, clinical data and the scores of the three questionnaires will be studied by conditional logistic regression models stratified by centre, and adjusted by arm (intervention vs control).

In the intervention arm, descriptive statistics will be presented on the satisfaction as well as on the number of interviews carried out and their average duration.

Ethics

The study will be conducted in accordance with the Declaration of Helsinki and the recommendations for Good Clinical Practice. Written informed consent will be signed by all study participants before enrolment in the study. Patients will have the right to withdraw from the study without incurring any prejudice at any time.

Patient involvement

RM, first author and expert patient, and members of DUP GA participated in the design of this study and will participate in all stages including teaching peers [23] and promoting and reporting the data, including publication in peer review. Thanks to training with health professionals and expert patients [22,23,25] peers will adopt the appropriate posture to enable patients to find their own resources to overcome barriers to use CPAP.

Dissemination

Dissemination plans of the results include presentations at conferences and a publication in peer-reviewed journal. Updates of the randomized trial will be available at ClinicalTrials.gov. All patients will be informed that the dissemination of results will be

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accessible on request.

Sponsor and funding

The study sponsor will be AGIR à dom. Co-Principal investigators are RM, an expert patient, and JCB, a researcher. The collaborators and sponsors were not involved in the design of the study and will not influence the execution, analysis or publication of results.

DISCUSSION

OSAS is associated with many negative health consequences [1]. The lack of compliance with home CPAP therapy, which is the first line of treatment, and which has shown to be effective on quality of life is a major issue both in terms of the patient's own health status and in health care utilisation [1,2,7,8]. Attempts have been made to improve CPAP compliance by improving technical issues relating to the comfort of use of the system [10,11] and the use of remote monitoring and telemedicine, along with the implementation of web-based adherence interventions [12–15]; however they have not been shown to improve compliance with the therapy. Other strategies to improve compliance therefore need to be developed and tested.

One of the main strengths of this study is the involvement of peers in the implementation of the behavioural intervention. Regarding efficacy, the involvement of patients with experience in the motivation of their peers to comply with treatment has been implemented with success in other chronic conditions requiring self-management such as HIV and diabetes [33,34]. Furthermore, evidence suggests that patients perceive peers with similar comorbidities as more credible than health-care professionals in the delivery of behavioural interventions [35–37]. The concept of PPI in education and research has been adopted by a growing number of medical schools, particularly in the United Kingdom [19,24]. If the results of this study confirm the effectiveness of the PI intervention in promoting

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resumption of CPAP in patients initially failing CPAP, this study will provide an evidence base to support the use of PI in the management of OSAS in conjunction with the home healthcare provider and specialized sleep centers [38].

The aim to seek factors that are related to CPAP resumption will provide useful information regarding those patients who are more likely to resume CPAP and therefore who PI interventions are more likely to help. This will open the way for further studies to determine the most appropriate methods to improve compliance in those patients who benefit less from PI interventions.

Despite these strengths, the study has two main inherent limitations. Firstly, the results are likely to be biased by the fact that patients who accept to participate may be more likely to resume CPAP therapy than those who decline participation. The results may therefore not be generalizable to all patients who have stopped using their CPAP as prescribed. Secondly, the effectiveness of the intervention may also depend on the capacity of the peer-participant to deliver it. The training is quite short (3 half-days) and some of the peers recruited may be more skilled than others in providing such intervention. However, in this study, the peers will be additionally supported throughout the study by the University Department of Patients.

In summary, the results of this study will determine the effectiveness of a PI intervention to motivate patients who have stopped using their CPAP as prescribed to resume its use on compliance with CPAP therapy. The results will also provide information regarding the factors relating to resumption of CPAP, providing a starting point for further studies to determine the most appropriate methods to improve compliance in those patients who benefit less from PI interventions.

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12
13
14 335 reviewing.
15
16 336
17
18 337 **Contributors** RM participated in the design of the study, wrote the article based on the
19
20
21 338 study protocol, will train PI, collect and analyse data into the protocol. CP participated in
22
23 339 the design of the study, wrote the study protocol and will include patients into the
24
25 340 protocol together with PPI. SL participated in the design of the study, wrote the study
26
27
28 341 protocol. CD and NA participated in establishing the sample size and will help to recruit
29
30 342 patients. MR set up statistical analysis plan and determine sample size. RT revised the
31
32 343 manuscript, will include patients into the protocol and collect and analyse data. JLP
33
34
35 344 designed the study, critically revised the manuscript, will include patients, and collect and
36
37 345 analyse data. JCB designed the study, critically revised the manuscript and will analyse
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39 346 data. The submitted manuscript has been approved by all authors.
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JLP received grants from Agir pour les Maladies Chroniques, <http://fonds-apmc.org/>.

Ethics approval

The protocol to be approved by The French Regional Ethics Committee CPP Ouest II-
Angers.

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499 **Table 1 -Inclusion and exclusion criteria**

| Inclusion criteria | Exclusion criteria |
|---|---|
| <ul style="list-style-type: none">Over 18 years' oldDiagnosed with of severe OSA (AHI \geq 30 events/hour)Discontinuation of CPAP 4 to 12 months after initiation, despite the interventions of health professionals and provider, and having stopped their CPAP treatment no later than one year prior to their inclusionFollowed by the home health care provider AGIRaDomAccess to a computer and/or tablet and an internet connectionOral and written FrenchAble to provide written informed consentAffiliated to social security or beneficiary of such a scheme | <ul style="list-style-type: none">CPAP cessation due to a resolution of the OSAS (e.g. weight loss after bariatric surgery) or another pathology that prevents the continuation of treatment (e.g. ENT surgery, etc.)Severe and/or unstable comorbidity that required hospitalization for decompensation in the previous year (heart, kidney, respiratory, liver, psychiatric or other insufficiency)Central sleep apnoea index above 20% of AHI at the time of diagnosisPatient being treated with a mandibular advancement orthosisLack of availability (e.g. night worker or patient who travels frequently, etc.).Current participation in, participation in the month prior to inclusion in another clinical intervention research study that may impact the study: this impact is left to the investigator's discretion.Referred to in Articles L1121-5 to L1121-8 of the CSP (corresponds to all protected persons: pregnant woman, breastfeeding mother, person deprived of liberty by judicial or administrative decision, person subject to a legal protection measure) |

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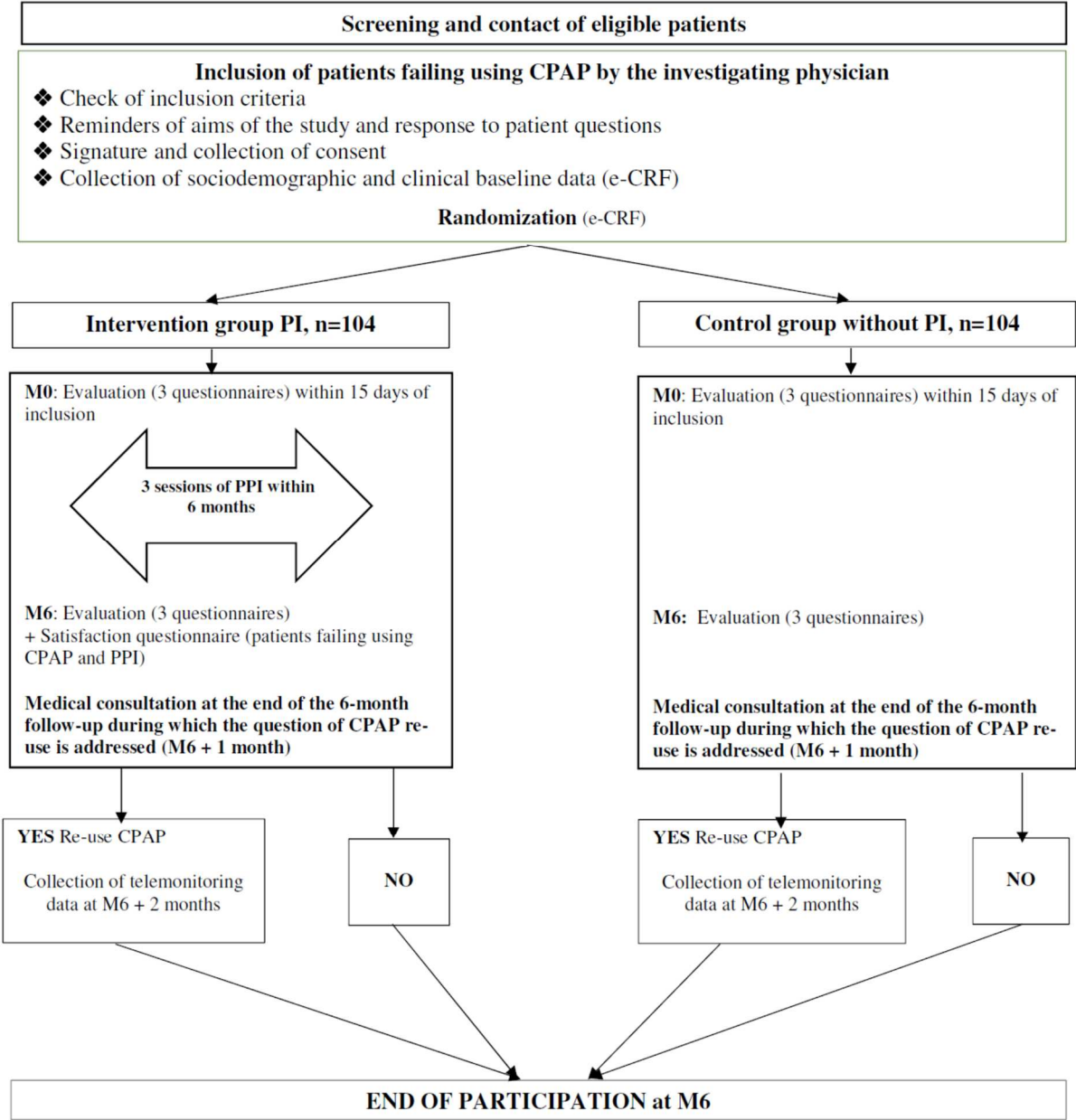
501 **Figure 1. Study design**

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Figure 1, Work-flow



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Supplementary file

SPIRIT 2013 Checklist

| Section/item | ItemNo, ligne manuscript | Description |
|--------------------------------------|----------------------------|--|
| Administrative information | | |
| Title | 1, 1-2 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym |
| Trial registration | 2a, 62 | Trial identifier and registry name. If not yet registered, name of intended registry |
| 2b, | | All items from the World Health Organization Trial Registration Data Set |
| Protocol version | 3, joined, 6-05-2021, v1.1 | Date and version identifier |
| Funding | 4, 284-6 | Sources and types of financial, material, and other support |
| Roles and responsibilities | 5a, 340-9 | Names, affiliations, and roles of protocol contributors |
| 5b, C. Pison, cpison@chu-grenoble.fr | | Name and contact information for the trial sponsor |
| 5c, none | | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities |
| 5d, PI as C. Pison | | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) |
| Introduction | | |
| Background and rationale | 6a, 86-124 | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention |
| 6b | | Explanation for choice of comparators |
| Objectives | 7, 135-149 | Specific objectives or hypotheses |
| Trial design | 8, Fig. 1 | Description of trial design including type of trial (eg, parallel group, crossover, |

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| 2 | | | |
| 3 | | | factorial, single group), |
| 4 | | | allocation ratio, and |
| 5 | | | framework (eg, superiority, |
| 6 | | | equivalence, noninferiority, |
| 7 | | | exploratory) |
| 8 | Methods: Participants, interventions, and outcomes | | |
| 9 | Study setting | 9, 152-5 | Description of study settings |
| 10 | | | (eg, community clinic, |
| 11 | | | academic hospital) and list of |
| 12 | | | countries where data will be |
| 13 | | | collected. Reference to where |
| 14 | | | list of study sites can be |
| 15 | | | obtained |
| 16 | | | |
| 17 | Eligibility criteria | 10, Table 1 | Inclusion and exclusion |
| 18 | | | criteria for participants. If |
| 19 | | | applicable, eligibility criteria |
| 20 | | | for study centres and |
| 21 | | | individuals who will perform |
| 22 | | | the interventions (eg, |
| 23 | | | surgeons, psychotherapists) |
| 24 | | | |
| 25 | Interventions | 11a, 157-191 | Interventions for each group |
| 26 | | | with sufficient detail to allow |
| 27 | | | replication, including how |
| 28 | | | and when they will be |
| 29 | | | administered |
| 30 | | | |
| 31 | 11b, NA | | Criteria for discontinuing or modifying |
| 32 | | | allocated interventions for a given trial |
| 33 | | | participant (eg, drug dose change in response |
| 34 | | | to harms, participant request, or |
| 35 | | | improving/worsening disease) |
| 36 | | | |
| 37 | 11c, Fig. 1 | | Strategies to improve adherence to |
| 38 | | | intervention protocols, and any procedures for |
| 39 | | | monitoring adherence (eg, drug tablet return, |
| 40 | | | laboratory tests) |
| 41 | | | |
| 42 | 11d, none | | Relevant concomitant care and interventions |
| 43 | | | that are permitted or prohibited during the trial |
| 44 | Outcomes | 12, 136-149 | Primary, secondary, and other |
| 45 | | | outcomes, including the |
| 46 | | | specific measurement variable |
| 47 | | | (eg, systolic blood pressure), |
| 48 | | | analysis metric (eg, change |
| 49 | | | from baseline, final value, |
| 50 | | | time to event), method of |
| 51 | | | aggregation (eg, median, |
| 52 | | | proportion), and time point |
| 53 | | | for each outcome. |
| 54 | | | Explanation of the clinical |
| 55 | | | relevance of chosen efficacy |
| 56 | | | and harm outcomes is |
| 57 | | | strongly recommended |
| 58 | | | |
| 59 | Participant timeline | 13, Fig. 1 | Time schedule of enrolment, |
| 60 | | | interventions (including any |

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| | | run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) |
| Sample size | 14, 220-8 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations |
| Recruitment | 15, 229-33 | Strategies for achieving adequate participant enrolment to reach target sample size |
| Methods: Assignment of interventions (for controlled trials) | | |
| Allocation: | | |
| Sequence generation | 16a, 235-6 | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions |
| Allocation concealment mechanism | 16b, 235-6 | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned |
| Implementation | 16c, 235-6 | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions |
| Blinding (masking) | 17a, NA except outcome assessors | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how |
| 17b, NA | | If blinded, circumstances under which unblinding is permissible, and procedure for |

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| 2 | | | |
| 3 | | | revealing a participant’s allocated intervention |
| 4 | | | during the trial |
| 5 | Methods: Data collection, management, and analysis | | |
| 6 | Data collection methods | 18a | Plans for assessment and |
| 7 | | | collection of outcome, |
| 8 | | | baseline, and other trial data, |
| 9 | | | including any related |
| 10 | | | processes to promote data |
| 11 | | | quality (eg, duplicate |
| 12 | | | measurements, training of |
| 13 | | | assessors) and a description of |
| 14 | | | study instruments (eg, |
| 15 | | | questionnaires, laboratory |
| 16 | | | tests) along with their |
| 17 | | | reliability and validity, if |
| 18 | | | known. Reference to where |
| 19 | | | data collection forms can be |
| 20 | | | found, if not in the protocol |
| 21 | | | |
| 22 | | | |
| 23 | 18b, 229-233 | | Plans to promote participant retention and |
| 24 | | | complete follow-up, including list of any |
| 25 | | | outcome data to be collected for participants |
| 26 | | | who discontinue or deviate from intervention |
| 27 | | | protocols |
| 28 | | | |
| 29 | Data management | 19, see Protocol | Plans for data entry, coding, |
| 30 | | | security, and storage, |
| 31 | | | including any related |
| 32 | | | processes to promote data |
| 33 | | | quality (eg, double data entry; |
| 34 | | | range checks for data values). |
| 35 | | | Reference to where details of |
| 36 | | | data management procedures |
| 37 | | | can be found, if not in the |
| 38 | | | protocol |
| 39 | | | |
| 40 | Statistical methods | 20a, 237-265 | Statistical methods for |
| 41 | | | analysing primary and |
| 42 | | | secondary outcomes. |
| 43 | | | Reference to where other |
| 44 | | | details of the statistical |
| 45 | | | analysis plan can be found, if |
| 46 | | | not in the protocol |
| 47 | | | |
| 48 | 20b, NA | | Methods for any additional analyses (eg, |
| 49 | | | subgroup and adjusted analyses) |
| 50 | | | |
| 51 | 20c, NA | | Definition of analysis population relating to |
| 52 | | | protocol non-adherence (eg, as randomised |
| 53 | | | analysis), and any statistical methods to |
| 54 | | | handle missing data (eg, multiple imputation) |
| 55 | Methods: Monitoring | | |
| 56 | Data monitoring | 21a, monitoring independant | Composition of data |
| 57 | | from investigators | monitoring committee |
| 58 | | | (DMC); summary of its role |
| 59 | | | and reporting structure; |
| 60 | | | statement of whether it is |

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independent from the sponsor
and competing interests; and
reference to where further
details about its charter can be
found, if not in the protocol.
Alternatively, an explanation
of why a DMC is not needed

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| 1 | 31-05-2021 version, <i>BMJ open Protocol-R2, revised document, the 4th of September 2021</i> | | |
| 2 | 21b, NA | | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial |
| 3 | | | |
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| 6 | Harms, NA | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct |
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| 10 | | | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor |
| 11 | | | |
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| 14 | Auditing | 23 every 3 months | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval |
| 15 | | | |
| 16 | | | |
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| 18 | | | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) |
| 19 | | | |
| 20 | | | |
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| 22 | Ethics and dissemination | | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) |
| 23 | Research ethics approval | 24, 267-271 | |
| 24 | | | |
| 25 | | | |
| 26 | Protocol amendments | 25, investigators | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable |
| 27 | | | |
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| 30 | | | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial |
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| 34 | | | Financial and other competing interests for principal investigators for the overall trial and each study site |
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| 38 | Consent or assent | 26a, patient's doctor | Statement of who will have access to the final trial dataset, and disclosure of |
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| 42 | 26b, NA | | |
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| 46 | Confidentiality | 27, | Financial and other competing interests for principal investigators for the overall trial and each study site |
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| 50 | | | Statement of who will have access to the final trial dataset, and disclosure of |
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| 54 | Declaration of interests | 28, 359-61 | |
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| 58 | Access to data | 29, investigators | |
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| Ancillary and post-trial care | 30, NA | contractual agreements that limit such access for investigators Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation |
| Dissemination policy | 31a, 279-82 | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions |
| 31b | | Authorship eligibility guidelines and any intended use of professional writers |
| 31c | | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code |
| Appendices | | |
| Informed consent materials | 32, protocol | Model consent form and other related documentation given to participants and authorised surrogates |
| Biological specimens | 33, NA | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable |

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SPIRIT 2013 Checklist

| Section/item | ItemNo, ligne manuscript | Description |
|--------------------------------------|----------------------------|--|
| Administrative information | | |
| Title | 1, 1-2 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym |
| Trial registration | 2a, 62 | Trial identifier and registry name. If not yet registered, name of intended registry |
| 2b, | | All items from the World Health Organization Trial Registration Data Set |
| Protocol version | 3, joined, 6-05-2021, v1.1 | Date and version identifier |
| Funding | 4, 284-6 | Sources and types of financial, material, and other support |
| Roles and responsibilities | 5a, 340-9 | Names, affiliations, and roles of protocol contributors |
| 5b, C. Pison, cpison@chu-grenoble.fr | | Name and contact information for the trial sponsor |
| 5c, none | | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities |
| 5d, PI as C. Pison | | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) |
| Introduction | | |
| Background and rationale | 6a, 86-124 | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention |
| 6b | | Explanation for choice of comparators |
| Objectives | 7, 135-149 | Specific objectives or hypotheses |
| Trial design | 8, Fig. 1 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, |

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| | | equivalence, noninferiority, exploratory) |
| Methods: Participants, interventions, and outcomes | | |
| Study setting | 9, 152-5 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained |
| Eligibility criteria | 10, Table 1 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) |
| Interventions | 11a, 157-191 | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered |
| 11b, NA | | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) |
| 11c, Fig. 1 | | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) |
| 11d, none | | Relevant concomitant care and interventions that are permitted or prohibited during the trial |
| Outcomes | 12, 136-149 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended |
| Participant timeline | 13, Fig. 1 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic |

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| | | diagram is highly recommended (see Figure) |
| Sample size | 14, 220-8 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations |
| Recruitment | 15, 229-33 | Strategies for achieving adequate participant enrolment to reach target sample size |
| Methods: Assignment of interventions (for controlled trials) | | |
| Allocation: | | |
| Sequence generation | 16a, 235-6 | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions |
| Allocation concealment mechanism | 16b, 235-6 | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned |
| Implementation | 16c, 235-6 | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions |
| Blinding (masking) | 17a, NA except outcome assessors | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how |
| 17b, NA | | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial |
| Methods: Data collection, management, and analysis | | |

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| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol |
| 18b, 229-233 | | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols |
| Data management | 19, see Protocol | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol |
| Statistical methods | 20a, 237-265 | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol |
| 20b, NA | | Methods for any additional analyses (eg, subgroup and adjusted analyses) |
| 20c, NA | | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) |
| Methods: Monitoring | | |
| Data monitoring | 21a, monitoring independent from investigators | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further |

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details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

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| 21b, NA | | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial |
| Harms, NA | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct |
| Auditing | 23 every 3 months | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor |
| Ethics and dissemination | | |
| Research ethics approval | 24, 267-271 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval |
| Protocol amendments | 25, investigators | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) |
| Consent or assent | 26a, patient's doctor | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) |
| 26b, NA | | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable |
| Confidentiality | 27, | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial |
| Declaration of interests | 28, 359-61 | Financial and other competing interests for principal investigators for the overall trial and each study site |
| Access to data | 29, investigators | Statement of who will have access to the final trial dataset, and disclosure of |

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| 6 | Ancillary and post-trial care | 30, NA |
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| 11 | Dissemination policy | 31a, 279-82 |
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| 23 | 31b | Authorship eligibility guidelines and any intended use of professional writers |
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| 24 | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code |
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| 31 | Appendices | |
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| 32 | Informed consent materials | 32, protocol |
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| 37 | Biological specimens | 33, NA |
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